

WHAT IS CLAIMED IS:

1. An isolated antigen-presenting cell for modulating an immune response, which is characterised by producing CD40, or its equivalent, at a level or functional activity that is less than about 50% of that produced by an activated dendritic cell.

5 2. An antigen-presenting cell according to claim 1, wherein CD40, or its equivalent, is produced at a level or functional activity that is less than about 1% of that produced by an activated dendritic cell.

3. An antigen-presenting cell according to claim 1, which cannot be induced to express CD40, or its equivalent, at an equivalent level and/or functional activity as that produced by an
10 activated antigen presenting cell.

4. An antigen-presenting cell according to claim 1, wherein CD40, or its equivalent, is produced at a level or functional activity that is lower than that produced by an immature dendritic cell.

5. An antigen-presenting cell according to claim 1, which cannot be induced to express
15 CD40, or its equivalent, at a higher level and/or functional activity than that produced by an immature antigen-presenting cell.

6. An antigen-presenting cell according to claim 1, which is other than a B lymphocyte.

7. An antigen-presenting cell according to claim 1, which is selected from monocytes, macrophages, cells of myeloid lineage, dendritic cells or Langerhans cells.

20 8. An antigen-presenting cell according to claim 1, which is a dendritic cell.

9. An antigen-presenting cell according to claim 1, which is a macrophage.

10. An antigen-presenting cell according to claim 1, which produces NF- κ B or a component thereof, at a level or functional activity which is lower than that produced by a mature or activated dendritic cell.

25 11. An antigen-presenting cell according to claim 1, which cannot be induced to express NF- κ B or component thereof, at a higher level and/or functional activity than an immature antigen presenting cell.

12. An antigen-presenting cell according to claim 1, which produces NF- κ B or a component thereof, at a level or functional activity that is lower than that produced by an immature dendritic
30 cell.

13. An antigen-presenting cell according to any one of claim 10 to 12, wherein the component is RelB.

14. An antigen-presenting cell according to claim 1, which produces an immunostimulatory molecule.

15. An antigen-presenting cell according to claim 14, wherein the immunostimulatory molecule comprises CD86 or its equivalent.

5 16. An antigen-presenting cell according to claim 14, wherein the immunostimulatory molecule is produced at a level or functional activity which is at least about 10% of that produced by an activated dendritic cell.

10 17. An antigen-presenting cell according to claim 14, wherein the immunostimulatory molecule is produced at a level or functional activity which is the same as that produced by an activated dendritic cell.

18. An antigen-presenting cell according to claim 1, which is produced by a process comprising contacting a precursor of the antigen-presenting cell with an NF- κ B inhibitor for a time and under conditions sufficient to differentiate an antigen-presenting cell from the precursor and to inhibit or otherwise reduce the level and/or functional activity of NF- κ B in the cell.

15 19. An antigen-presenting cell according to claim 18, wherein the precursor is derived from monocytes or bone marrow.

20. An antigen-presenting cell according to claim 18, wherein the NF- κ B inhibitor inhibits nuclear translocation of NF- κ B, or a component thereof.

20 21. An antigen-presenting cell according to claim 18, wherein the NF- κ B inhibitor inhibits nuclear translocation of RelB.

22. An antigen-presenting cell according to claim 18, wherein the NF- κ B inhibitor is an antisense nucleic acid molecule or oligonucleotide, which is complementary or encodes at least a portion of a NF- κ B subunit selected from p50, p65 or RelB.

25 23. An antigen-presenting cell according to claim 18, wherein the NF- κ B inhibitor is an inhibitor of RelB or p50.

24. An antigen-presenting cell according to claim 18, wherein the NF- κ B inhibitor is an inhibitor of RelB or p50, which is selected from a ribozyme that selectively destroys RNA encoding NF- κ B or component thereof, an antisense molecule which prevents transcription of NF- κ B or component thereof, or an antigen-binding molecule that blocks NF- κ B action.

30 25. An antigen-presenting cell according to claim 18, wherein the NF- κ B inhibitor is an indirect inhibitor of NF- κ B selected from inhibitors of I κ B degradation, inhibitors of I κ B phosphorylation, inhibitors of I κ B ubiquitination and inhibitors of proteolytic degradation of I κ B.

26. An antigen-presenting cell according to claim 18, wherein the NF- κ B inhibitor is an inhibitor of I κ B phosphorylation.

27. An antigen-presenting cell according to claim 18, wherein the NF- κ B inhibitor is BAY 11-7082.

5 28. An antigen-presenting cell according to claim 18, wherein the NF- κ B inhibitor is an indirect inhibitor of NF- κ B selected from inhibitors of proteolysis and inhibitors of nuclear translocation of NF- κ B.

29. An antigen-presenting cell according to claim 18, wherein the NF- κ B inhibitor is an inhibitor of nuclear translocation of NF- κ B selected from deoxyspergualin or deoxyspergualin
10 derivatives or analogues.

30. An antigen-presenting cell according to claim 18, wherein the NF- κ B inhibitor is an inhibitor of proteolysis selected from proteasome inhibitors.

31. An antigen-presenting cell according to claim 18, wherein the NF- κ B inhibitor is a proteasome inhibitor selected from PSI, ALLN, lactacystin, MG-132, C-LFF and calpain
15 inhibitors.

32. An antigen-presenting cell according to claim 18, wherein the NF- κ B inhibitor is an indirect inhibitor of NF- κ B selected from caffeic acid phenethyl ester, pyrrolidine dithiocarbonate, lovastatin, aselastine HCL, tepaxalin, (-)-epi gallocatechin-3-gallate, phenyl-N-tert-butyl nitron, quercetin, cucumin or E330.

20 33. An antigen-presenting cell according to claim 18, wherein the NF- κ B inhibitor inhibits proteolysis.

34. An antigen-presenting cell according to claim 18, wherein the NF- κ B inhibitor is a proteasome inhibitor.

35. An antigen-presenting cell according to claim 1, which is produced by a process
25 comprising contacting an antigen-presenting cell, or its precursor, with an inhibitor of CD40, or its equivalent, for a time and under conditions sufficient to produce a modified antigen-presenting cell that produces CD40, or its equivalent, at a reduced or abrogated level or functional activity relative to that of the antigen-presenting cell or its precursor.

36. An antigen-presenting cell according to claim 35, wherein the process further comprises
30 contacting the antigen-presenting cell, or its precursor, or the modified antigen-presenting cell, with an agent that increases the level or functional activity of an immunostimulatory molecule for a time and under conditions sufficient to enhance or otherwise elevate the level or functional activity of the immunostimulatory molecule in the antigen-presenting cell, or its precursor, or the modified antigen-presenting cell.

37. An antigen-presenting cell according to claim 35, wherein the process further comprises contacting the antigen-presenting cell, or its precursor, or the modified antigen-presenting cell, with an agent that increases the level or functional activity of CD86 or its equivalent, for a time and under conditions sufficient to enhance or otherwise elevate the level or functional activity of CD86 or its equivalent in the antigen-presenting cell, or its precursor, or the modified antigen-presenting cell.

38. A method of producing antigen-presenting cells for modulating an immune response to a target antigen, comprising contacting an antigen-presenting cell, or its precursor, with an antigen that corresponds to the target antigen, or with a polynucleotide from which the antigen is expressible, for a time and under conditions sufficient for the antigen or a processed form thereof to be presented by the antigen-presenting cell, or its precursor, wherein antigen-presenting cell, or its precursor, is characterised by producing CD40, or its equivalent, at a level or functional activity that is less than about 50% of that produced by an activated dendritic cell.

39. A method according to claim 38, wherein the antigen presentation is restricted by major histocompatibility (MHC) molecules.

40. An antigen-specific antigen-presenting cell for modulating an immune response to a target antigen, which is produced by contacting an antigen-presenting cell, or its precursor, with an antigen that corresponds to the target antigen, or with a polynucleotide from which the antigen is expressible, for a time and under conditions sufficient for the antigen or a processed form thereof to be presented by the antigen-presenting cell, or its precursor, wherein antigen-presenting cell, or its precursor, is characterised by producing CD40, or its equivalent, at a level or functional activity that is less than about 50% of that produced by an activated dendritic cell.

41. A method of producing antigen-presenting cells for modulating an immune response to a target antigen, comprising contacting a precursor of the antigen-presenting cell with an NF- κ B inhibitor and with an antigen that corresponds to the target antigen, or with a polynucleotide from which the antigen is expressible, for a time and under conditions sufficient to differentiate an antigen-presenting cell from the precursor and to inhibit or otherwise reduce the level or functional activity of NF- κ B in the cell, wherein the antigen or a processed form thereof is presented by the antigen-presenting cell so produced.

42. A method according to claim 41, wherein the immune response is mediated by T lymphocytes.

43. A method according to claim 41, wherein the T lymphocytes are selected from cytotoxic T lymphocytes (CTLs) and T helper lymphocytes.

44. A method according to claim 41, wherein the antigen is selected from a protein antigen, a particulate antigen, an alloantigen, an autoantigen, an allergen, a bacterial antigen, a viral antigen or a parasitic antigen or immune complex.

5 45. A method according to claim 41, wherein the modulation of the immune response is selected from inducing a tolerogenic response, or the suppression of a future or existing immune response, to a specified antigen or group of antigens.

10 46. A method for producing T lymphocytes that exhibit anergy for a target antigen, comprising contacting a population of T lymphocytes, or their precursors, with an antigen-specific antigen-presenting cell, which is characterised by producing CD40, or its equivalent, at a level or functional activity that is less than about 50% of that produced by an activated dendritic cell, for a time and under conditions sufficient to produce the anergic T lymphocytes.

47. A method according to claim 46, wherein the T lymphocytes are selected from cytotoxic T lymphocytes (CTLs) and T helper lymphocytes.

15 48. A method according to claim 46, wherein the antigen is selected from a protein antigen, a particulate antigen, an alloantigen, an autoantigen, an allergen, a bacterial antigen, a viral antigen or a parasitic antigen or immune complex.

20 49. A T lymphocyte that exhibits anergy for a target antigen, which is produced by contacting a T lymphocyte, or its precursor, with an antigen-specific antigen-presenting cell, which is characterised by producing CD40, or its equivalent, at a level or functional activity that is less than about 50% of that produced by an activated dendritic cell, for a time and under conditions sufficient to produce the anergic T lymphocyte.

25 50. A method for modulating the immune response to an antigen, comprising administering to a patient in need of such treatment an antigen-specific antigen-presenting cell for a time and under conditions sufficient to modulate the immune response, wherein the antigen-specific antigen-presenting cell is produced by contacting an antigen-presenting cell with an antigen that corresponds to the target antigen, or with a polynucleotide from which the antigen is expressible, for a time and under conditions sufficient for the antigen or a processed form thereof to be presented by the antigen-presenting cell, wherein antigen-presenting cell is characterised by producing CD40, or its equivalent, at a level or functional activity that is less than about 50% of that produced by an activated dendritic cell.

30 51. A method for modulating the immune response to an antigen, comprising administering to a patient in need of such treatment an anergic T lymphocyte for a time and under conditions sufficient to modulate the immune response, wherein the anergic T lymphocyte is produced by contacting a population of T lymphocytes, or their precursors, with an antigen-specific antigen-presenting cell, which is characterised by producing CD40, or its equivalent, at a level or functional

activity that is less than about 50% of that produced by an activated dendritic cell, for a time and under conditions sufficient to produce the anergic T lymphocytes.

52. Use of an antigen-specific antigen-presenting cell according to claim 40 and/or of an anergic T lymphocyte according to claim 49 for inducing an anergic response.

5 53. Use of an antigen-specific antigen-presenting cell according to claim 40 and/or of an anergic T lymphocyte according to claim 49 for treating or preventing an allergy.

54. Use of an antigen-specific antigen-presenting cell according to claim 40 and/or of an anergic T lymphocyte according to claim 49 for treating or preventing an autoimmune disease.

10 55. Use of an antigen-specific antigen-presenting cell according to claim 40 and/or of an anergic T lymphocyte according to claim 49 for treating or preventing transplant rejection in a patient.

56. A method for treatment and/or prophylaxis of a disease or condition whose symptoms or aetiology are associated with the presence of an immune response, comprising administering to a patient in need of such treatment or prophylaxis an effective amount of one or both of an antigen-specific antigen-presenting cell according to claim 40 and/or of an anergic T lymphocyte according to claim 49 .

57. Use of an antigen-specific antigen-presenting cell according to claim 40 and/or of an anergic T lymphocyte according to claim 49 in the preparation of a medicament for the modulation of an immune response.

20 58. Use of an antigen-specific antigen-presenting cell according to claim 40 and/or of an anergic T lymphocyte according to claim 49 in the study and modulation of immune responses.